Instruction For Use
Najuta CMD Thoracic Stent Graft System
(Custom-made device)

- **SINGLE USE ONLY,Reuse of this device may cause communication of disease both to patients and users. If the device is reused, the dimensions and shape of the re-used device does not match with aortic shape of a patient and it may cause serious complication such as cerebrovascular disease, thromboembolism and so on. These risks may lead to death.**

- **STERILE – DO NOT RESTERILIZE**

1. Warning

1.1. Application (patient)

(1) Because long-term records of endovascular repair using stent grafts are not established at present, the imaging diagnosis shall be regularly performed. The patients, whose lesion was treated by this device, should receive follow-up to assess the status of the implanted stent graft and the size of the lesion even when the patient does not have symptoms such as pain, paralysis, hoarseness.

(2) Because this device is designed to be implanted and used in a blood vessel, and may cause metal allergy caused by Stainless Steel (Fe, Ni, Mo, Cr etc), the validity of endovascular repair shall be reviewed for a patient with metal allergy.

(3) The application of this device to a patient for whom the insertion of a delivery sheath is not suited due to an occlusion, significant calcification, and tortuous artery shall be avoided.

(4) The application of this device to a patient who has significant calcification, a mural thrombus, or a mural atheroma at the site where a stent graft is intended to be fixed shall be avoided.

(5) At the CT/CTA diagnosis in the postoperative follow-up, assessment even with multi-axis shall be considered to grasp the expansion tendency of diameter of lesion. [In the clinical trial of the similar medical device, aneurysm expansion was observed for aortic aneurysm in the body axis direction.]

(6) When used for dissection, remodeling of blood vessels can shift the position of the fenestration.

(7) An insufficient oversizing rate may increase the incidence of Type I EL.

(8) Because safety and effectiveness have not been established on some indications for the custom made device, special consideration about risk and benefit is required.

1.2. Operational and clinical

(1) Facilities where the endovascular repair using this device is conducted shall have the system and infrastructure as follows:

- A DSA apparatus must be installed in an operating room or an angiography room with proper hygiene where emergency surgery can be provided. In addition, the facility must have a system that allows aortic surgery.
- In preparation for the need of shifting to surgical thoracotomy during the implantation procedures of this device, sufficient medical equipment and medical system shall be present as well as cooperation of a surgeon who has experienced great vessel surgery.

(2) Physicians who perform the endovascular repair using this device shall fill the requirements as follows:

- The Najuta CMD Thoracic Stent Graft System should only be used by physicians, who have knowledge and experience about endovascular repair, which the manufacturer requires.
- The physicians shall have substantial experiences in imaging diagnosis regarding endovascular repair and endovascular repair itself (and shall have knowledge about selecting specifications of stent grafts on the basis of information obtained from interpretation of radiogram and images).
- The physicians shall have thoroughly completed the physician training program for this Najuta CMD Thoracic Stent Graft System (including lecture, visit and see actual operation or watch operation movie, actual clinical operation) , provided by the manufacturer.

(3) In case a malapposition occurs on the proximal end of this device, it may lead to breakage or deformation of the device. To avoid this, on selecting specification, a proper one suited to vessel size shall be selected, taking notice

that a proximal diameter of stent graft should not be smaller than vessel diameter where the device is implanted. If striking malapposition is observed under or after operation, even though fluctuation of stent graft is not found under controlled blood pressure during operation, postoperatively significant fluctuation may happen and it can lead to breakage or collapse of stent graft. Therefore in such a case, appropriate additional treatment and careful follow-up shall be done. [In clinical use of the similar medical device, it was confirmed that a case with significant malapposition on the proximal end of stent graft resulted into deformation and breakage of stent graft. It was caused because blood flew into between stent graft and vessel wall and then fluctuation and collapse of stent graft occurred postoperatively.] [Referring to "6.2. Appropriate device selection"]

(4) Once deployment of stent graft is started, do not change the position of the stent graft (re-position after being completely deployed) or draw it back into the sheath (re-sheath) . Do not deliver the delivery system forward to the proximal side with the stent graft exposed from the outer sheath. [That is because if the stent graft is placed while it is pulled, there is a risk of deformation of the stent resulting in awkward shape, vascular injury, or implanting of the stent graft in a wrong position.]
[There is a risk of occlusion of branch vessels, perforation of aortic walls caused by the stent graft, endoleak, stent collapse, and others because of implantation failure.]

(5) As this device has inner skeleton (stent skeleton is placed inside of graft), delivery sheath may be captured by stent skeleton when it goes through inside of the device. Therefore, insertion and removal of delivery sheath requires careful operation under enlarging fluoroscopic view for the tip being not to be captured by skeleton. [Referring "How to use, 6.6(3)]

(6) In case Left subclavian artery is covered by implantation of this device, be sure to perform necessary medical assessment in advance (assessment of the need for transposition of the artery or bypass surgery).

(7) When the proximal end of the stent graft reaches Zone 1, or the proximal end of the stent graft covers the arch branch vessel that is not intended, the pulses of both right and left carotid arteries shall be checked by palpation or other ways immediately after implantation of the stent graft. If a pulse cannot be felt, the left common carotid artery or brachiocephalic artery can be occluded for some reason, and immediately check the blood flow of the arch branch vessel under angiography. If the occlusion of the branch vessel is observed, appropriate treatment should be performed promptly. [Occlusion of the arch branch vessel may incur the risk of causing a serious event such as death, cerebral infarction.How to prevent, refer to "6.6 Insert and remove a device (3) Contrast imaging for confirmation and implantation of stent graft" and "6.6 Insert and remove a device (4) Implantation of stent graft having fenestration"]

(8) After an implantation, follow up should be performed. When and how should be based on a protocol of each hospital. In the clinical trial of the similar medical device, the first follow up was performed at discharge and surveillance was repeated after 3 months, 6 months, 12months, then yearly. Detailed examination shall be immediately conducted for a patient who shows conspicuous lesion expansion (5 mm or more in the case of aortic aneurysm), a sustained endoleak and appearance of a new endoleak, or migration of the stent graft leading to insufficient sealing of lesion. Accordingly additional endovascular treatment or conversion to regular open surgery shall be considered for them [That is because aneurysm expansion or appearance of endoleak may lead to aneurysm rupture.]
If invagination of the stent graft into the aneurysm or compression of the stent graft is observed, endovascular treatment or immediate conversion to open surgery for recovering blood flow should be considered .

2. Contraindication

2.1. Application (patient)

(1) Do not use this device for diseases other than thoracic aortic disease that fills anatomical requirements.

(2) Do not use this device for the patients who are allergic or sensitive to PTFE, stainless steel, and polyvinylidene fluoride.

(3) This device should not be applied to patients who cannot receive preoperative and postoperative imaging diagnosis and postoperative follow-up (See more detail in 9.Image diagnosis), who cannot fill imaging requirements because of excessive weight or height, and who do not approve of receiving preoperative and postoperative imaging diagnosis and postoperative follow-up.

(4) This device should not be applied to patients to whom a contrast agent cannot be used for imaging diagnosis at operation or during follow-up.

2.2. Operational and clinical

(1) Do not reuse, do not re-sterilize, single use only.

(2) Do not dip this device into a medicine containing an organic solvent such as rubbing alcohol or wipe this device using such a medicine. [Failure to observe this may damage or cut this device.]

2.3. Relative Contraindication

In principle, this device shall not be used for the following patients, however, it shall be used with extra care as specifically necessary.

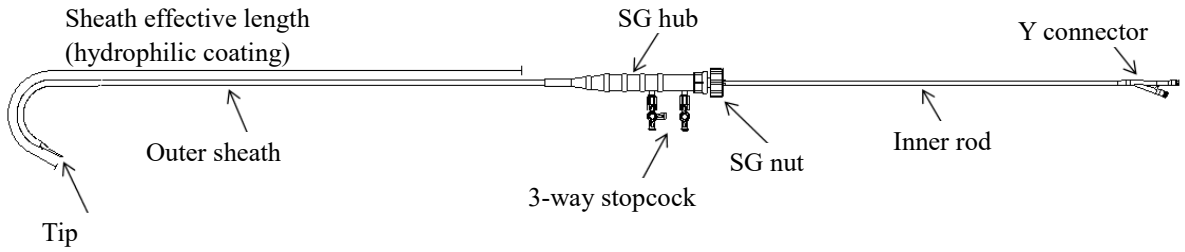
For the patients applicable to the following items, the safety and effectiveness of this device are not evaluated.

- Acute dissection
- Aorta fistula
- Aortitis or inflammatory aortic aneurysm
- Infected aneurysm
- Aneurysm rupture
- Traumatic aortic interruption
- Congenital connective tissue disorder(Marfan syndrome, Ehlers-Danlos syndrome)
- Patients with active systemic infection
- Patients with cerebral vascular accident (CVA) within 3 months from occurrence
- Patients of less than 20 years old
- Patients who are pregnant or in nursing [concern about effect on fetus caused by X-ray]

3. Shape, structure, principle, etc.

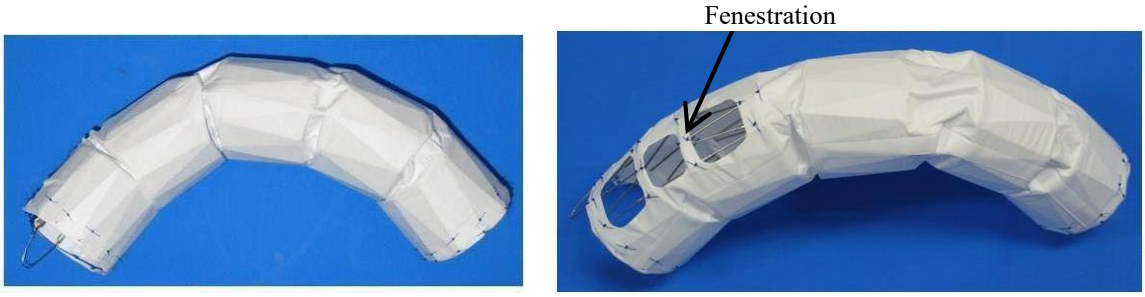
3.1. Structural drawing

1. Delivery sheath



Materials of the delivery sheath: polyamide elastomer, polyethylene,Polypropylene, stainless steel,Polycarbonate
Hydrophilic coating material: polyvinylpyrrolidone

2. Stent graft



Materials of the stent graft: polytetrafluoroethylene, stainless steel,Polyvinylidene fluoride

3.2. Principle

This stent graft consists of a stent made of stainless steel and a polytetrafluoroethylene graft sewn on the stent.The device is filled into the delivery sheath in advance and after being carried to the aimed vessel site of the thoracic aorta, deployed from the delivery sheath for implanting. The stent graft is self-expanded to a specified diameter, seal closely to the vessel wall.

The specifications with 1 to 3 fenestration(s) make it possible to implant reaching ascending aorta without blocking blood flow into branch vessel (brachiocephalic artery, common carotid artery, etc.), by placing fenestrations under the branch vessel of the aimed lesion at the aortic arch.

4. Intended use, Indications

This device is indicated for endovascular repair of patients having thoracic aortic disease who meet anatomical conditions described in below.

(1) Appropriate iliac /femoral artery access route shall be present.
(2) A normal vessel as sealing zone at both the proximal side and distal side of the lesion area shall be present.
(3) The diameter of the normal blood vessel at the fixation zone of the proximal side and distal side of the lesion area shall be 20 mm or larger but less than 42 mm.

Caution: Atheroma or similar deposition on vessel wall may lead to endoleak.

Caution: Aortic disease includes the following: thoracic aortic aneurysm, pseudoaneurysm, aortic dissection, patent ductus arteriosus, and penetrating atherosclerotic ulcer. For some of aortic diseases, the long-term safety and effectiveness of this device has not been established. Diseases that require specific attention are listed in Section 2.3, Relative Contraindication.

5. Specifications and more

5.1. Specifications of stent graft

(1) Joint strength of stent
The following strength shall be guaranteed when each joint (swaged point) of the stent skeleton is pulled in the length direction.

Joint	Minimum joint strength
Bent joint of stent	60N
Joint between bent and strut	
Joint between bent and hook	
Joint between bent and fin	

(2) Seal strength of graft
The seal strength of 10N or higher shall be guaranteed when the seal of the graft is cut by 1cm.

(3) Pressure resistance
No damage is caused when 200mmHg of pressure is applied to the graft.

5.2. Specifications of delivery sheath

(1) Joint strength of delivery sheath
The following strengths shall be guaranteed when each joint (swaging) of this device is pulled in the length direction.

Joint	Minimum joint strength
Between inner rod and Y connector	15N
Between outer sheath and SG hub	15N
Between inner rod and shaft pipe	10N
Between tip and shaft pipe	10N

The outer diameter presented at the minimum bonding strength is a smaller outer diameter of bonded inner rod or shaft pipe.

(2) Maximum applicable guide wire diameter
0.035 inches (0.89mm) or smaller

6. Operation and how to use

6.1. Materials to be prepared

- Heparin and heparinized saline
- Angiographic catheter (pigtail catheter recommended)
- Guidewire
  -For through and through: angiographic guidewire with diameter of up to 0.035 inches and length of 4.0m recommended
  -For angiographic catheter guide: guidewire with diameter of up to 0.035 inches and length of 1.5m or longer recommended
  -For balloon catheter: stiff wire with diameter of up to 0.035 inches and length of 2.5m or longer recommended
- Sheath introducer
  (For brachial artery: 6Fr, for common femoral artery: 8 - 10Fr recommended)
- Snare catheter recommended
- Sterile syringe (20cc or larger for flush recommended)
- Balloon catheter with appropriate diameter
- Appliances and medication in general for angiography
- Surgical instruments in general required for reaching ex. femoral artery access vessel and incision.

6.2. Appropriate device selection

A device shall be selected on the basis of the CT image (slice thickness of 2mm or thinner) obtained within 6 months in prior to the scheduled implanting date.

6.2.1 Implantation area

(1) If the distance between the main branch and aortic lesion is long enough, the implanting range shall be planned to secure the stent graft fixation zone of 6cm or longer at both the proximal side and distal side to the extent possible regardless of the length of the aortic lesion.
(2) If the length of the aortic aneurysm lesion exceeds 5cm, 2 or more stent grafts shall be used connected in the aortic aneurysm. For connecting use, the overlapped portion shall be planned to be 6cm or longer.
(3) The stent graft shall be planned to be implanted along the greater curvature side as much as possible in consideration of the change of aortic morphology at the late period.

6.2.2. Selection of device to be used

- The matallic stent having 3 dimentional curve that is best approximation to the aortic shape of the planned implanting area shall be selected on the basis of 3D-CT image.
- The stent selection shall start with check of anteroposterior curve of the aorta in the stent graft implanting area. The selection shall be narrowed to the skeletons of which anteroposterior sharp curve can be placed to the that of aorta. (More curve portions are often observed from the aortic arch to descending aorta and on the diaphragm).
- The torsion of the aorta in the stent graft implanting area shall be checked. Torsion to the back side at the distal arch and torsion to the back side at the diaphragm lacuna from the descending aorta to thoracoabdominal portion are anatomically often observed.
- The selection of stents with the most approximate shape shall be selected on the basis of the aorta torsion among specifications narrowed on the basis of anteroposterior curve. Thus final selection of a stent to be used shall be decided.
- Regardless of fenestrated or not fenestrated is the stent graft to be used, the diameter of the stent graft is prefered to exceed the size of the vessel diameter at the fixation zone by 10% to 15%. If proximal side and distal side have different vascular diameter at each fixation zone, the diameter of the stent graft shall be selected according to the larger vessel diameter. However, if the diameter of the selected stent graft exceeds the smaller vessel diameter at the fixation point by 15% or more, the use of tapered type shall be considered.
- If a satisfactory proximal fixation zone of 25mm or longer cannot be secured at the distal side of the bifurcation of left subclavian artery, the stent graft with fenestration(s) shall be used to expand the length of the fixation zone by positioning fenestration(s) under the carotid and brachiocephalic artery. If it is decided left subclavian artery shall not be covered by stent graft, the use of a stent graft with fenestration(s) positioning fenestration(s) under the left

subclavian artery shall be considered.

- Though the length between the bifurcation of left subclavian artery to lesion is simply 25mm or more, if it is judged that a satisfactory sealing zone of 25mm or longer cannot be secured at the lesser curvature side due to strong torsion from the immediate below the left subclavian artery to descending aorta, specifications with fenestration(s) shall be used.
- If a specification having fenestrations on a strut (2 or 3 fenestration specification) is used and placed to keep open a branch vessel, the implanting position of the stent graft shall be planned so that a sealing zone built with a Z stent skeleton and the normal blood vessel is established between the fenestration on the strut and aneurysm.

Caution: Sealing built only with a Z stent skeleton and a strut connecting the Z stent skeleton may cause endoleak.

Caution: If the exceed size of the stent graft diameter to the vessel diameter in the fixation zone is less than 10%, safety assessment has not been established.

6.2.3. Multiple use of Najuta CMD Thoracic Stent Graft System

(1) When 2 pieces of Najuta CMD Thoracic Stent Graft System with the same diameter are used

• It is advisable to insert a stent graft at the proximal side after placing a stent graft at the distal side in consideration of resistance caused by blood flow.

(2) When 2 pieces of Najuta CMD Thoracic Stent Graft System with different diameters are used

• When stent grafts each of which has a different diameter are used, those grafts can be connected if the diameters of those grafts are within 2 sizes.

• The stent graft with smaller diameter shall be placed first, and then another stent graft with larger diameter shall be implanted.

(3) When 3 pieces or more of Najuta CMD Thoracic Stent Graft System are used

• A stent graft with the diameter of up to 2 sizes larger than the smaller diameter between other two overlapping stents already implanted can be used as the third stent graft.

• Even when 3 or more stent grafts are used, a stent graft with larger diameter shall be always implanted in a stent graft with smaller diameter.

Caution: Combined use with the device from other stent-graft is not verified.

6.3. Confirmation for anatomical applicability

The following points shall be preoperatively confirmed for anatomical applicability of this device:

(1) No occlusion, conspicuous calcification, or tortuosity shall be found in the access vascular.

(2) Diameter of fixation zone shall be in the range 20-42mm.

6.4. Vascular access

(1) Expose the femoral artery or iliac artery by a small incision of the groin according to the standard procedure, and secure the access vascular to insert this device. Insert a sheath introducer into the right brachial artery to secure the secondary access site for through and through, diagnosis, and contrast imaging.

(2) Administer an anticoagulant systemically according to the standard procedure to provide anticoagulant therapy for reducing the risk of thromboembolism.

6.5. Device preparation

(1) Take out this device from the packaging material under aseptic conditions. If a resistance is felt at the time of taking this device from the package, check whether the delivery sheath or other items are not deformed and any part of them is not detached. [Be careful to take out this device in order not to be caught on the tray.

(2) Make sure that the SG nut is tightened enough and tighten it as necessary.

(3) Ensure if 1 way-cock and 3 way cock are tightened and if not tighten it. Then expel the air from the inside of the outer sheath using the syringe with heparinized saline contained. Replace the air in the outer sheath with heparinized saline completely by injecting heparinized saline from the proximal port of the outer sheath. Repeat flushing until no bubble is observed in the heparinized saline coming from the side hole at the tip of the outer sheath. Lock the cock after the air in the outer sheath is completely replaced with the heparinized physiological saline.

(4) Expel the air in the inner rod with heparinized saline completely by injecting it from the Y connector at the distal side of the inner rod in the same way.

6.6. Insert and remove a device

(1) Guidewire insertion for the through and through technique

- Insert a through and through guidewire from the sheath introducer at the secondary access site prepared at the right brachial artery and lead the through and through guidewire into the aorta by the angiographic catheter or guiding catheter, etc. On the other hand, insert a sheath introducer into the access vascular of the femoral artery and insert a snare catheter. Capture the tip of the through and through guidewire with the snare catheter in the aorta under X-ray angiography and remove the snare catheter slowly. When the tip of the guidewire is captured with the snare catheter, be careful not to kink the guidewire. If the guidewire is kinked, it cannot pass through the guidewire lumen of the stent graft delivery sheath.
- This operation can lead the tip of the through and through guidewire, which was inserted from the secondary access site of the right brachial artery, to the outside of the body through the access vascular of the femoral artery, and the preparation for the through and through technique has been completed. The through and through procedure, incidentally, can be performed without using a snare catheter. In that case, insertion of a sheath introducer into the femoral artery is not necessary, and an operation procedure that is standard in each facility shall be followed.
- When the access from the right brachial artery cannot be provided, the through and through technique from the left brachial artery can be performed only in the case that treatment is possible without delivering the tip of delivery sheath from the bifurcation of the left subclavian artery to the proximal side.

(2) Delivery of stent graft

- Remove the sheath introducer inserted in the access vascular, at the same time, shut the proximal and distal sides of the access vascular with a forceps, and leave only the through and through guidewire. Insert the through and through guidewire into the guide wire lumen at the tip of the stent graft delivery sheath and pull out from the Y connector at the edge of the stent graft delivery sheath.
- Partly incise the access vascular at the site where the sheath introducer was inserted, and insert the delivery sheath carefully into the blood vessel under the guidance of the through and through guidewire. At that time, contact between the vessel inner wall and delivery sheath should be completely close using a tourniquet in order for avoiding bleeding from the space between the vessel inner wall and delivery sheath.
- After insertion into blood vessel, move the delivery sheath to the planned implanting position under X-ray angiography under properly adjusted tension of through and through guidewire by pulling both the proximal and distal sides of it.
- When the tip of the delivery sheath reaches Zone 2, the tension of the through and through guidewire shall be adjusted in order for the tip of the delivery sheath not to damage the arch greater curvature side. When the tip of the delivery sheath reaches Zone 0, guidewire shall be kept in the state of sagging in the ascending aorta. Only under this state of guidewire, the delivery sheath shall be moved forward.

Caution: If a resistance is felt in delivering a delivery sheath to the implanting position, stop moving it forward and find the cause under X-ray fluoroscopy. Failure to observe this may cause vascular injury, damage to the stent graft system, peeling of the coat on the through and through guidewire, and more. Do not pull the through and through guidewire excessively. Failure to observe this may cause vascular injury, damage to the stent graft system, and fracture of the guidewire.

(3) Contrast imaging for confirmation and implantation of stent graft

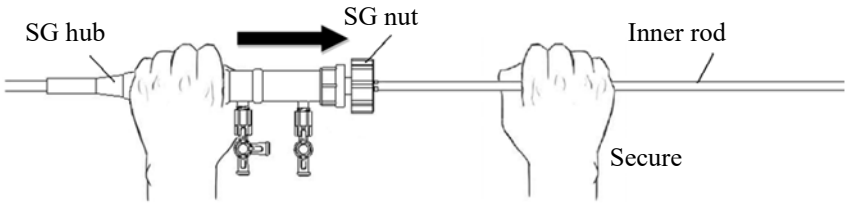
- Insert a guidewire (for angiographic catheter guide) newly from the sheath introducer at the secondary access site, and lead an angiographic catheter to the thoracic aorta. Then perform contrast imaging for confirmation at the site where a stent graft is planned to be implanted.

Caution: Reconfirm that the specification of the selected stent graft is proper by confirming front and rear of the lesion under fluoroscopy.

- Using the radiopaque markers of the stent graft as marks, determine the implanting position of the stent graft by comparing the preoperatively planned implanting position with the DSA imaging data for confirmation. Confirm also that the rotation direction is appropriate.
- After determination of the implanting position, loosen the SG nut that secures the inner rod, hold the SG hub of the delivery sheath and slowly move it in the arrow direction as shown in the drawing below while observing the position of the radiopaque markers of the stent graft under X-ray fluoroscopy, and the stent graft is gradually

deployed.

(Figure)



SG hub: hub for stent graft
SG nut: nut for stent graft

Caution: In case stent graft is implanted at curvature part such as ascending aorta, arch of aorta, delivery sheath shall stay along the greater curvature side when stent graft is released. If the delivery sheath is not along and on the greater curvature on deployment, risk of malaposition is increased. [Occurrence of malapposition may lead to fluctuation of stent graft, collapse of stent graft and breakage of skeletons]

Caution: After starting release of stent graft, an operator should adjust finely the position of implantation (e.g. fenestration) by manipulating the delivery sheath under backward blood flow pressure.（Minor adjustment is possible until the 4th stent starts to be released)

Caution: When the position of the secured inner rod moves, the position of the stent graft also moves. Quick movement of the inner rod may displace the stent graft from the planned implantation position and bend the inner rod, resulting in that stent graft cannot be successfully deployed.

- If a high resistance is felt when the outer sheath starts to be moved, pull the SG hub back slowly after holding the inner rod in proximity of the SG nut. Once the stent graft is deployed from the outer sheath, it becomes uncollectible.
- After release and deployment of the stent graft under X-ray fluoroscopy, remove the stabilizer line from the Y connector. Evulsion of the stabilizer line shall be performed with the inner rod being firmly secured to prevent stent graft from moving.
- After placement of the stent graft and removal of the stabilizer line, pull the inner rod to the distal side slowly and release the tip of the delivery sheath from the stent graft hook. (If the specification which the stent graft hook is not attached to the tip of the delivery sheath is used, this step is omitted.)
- Pull the inner rod slowly while using caution to prevent the tip of the delivery sheath from being caught by the implanted stent graft to retract the tip into the outer sheath. Tighten the SG nut to secure the inner rod and remove the delivery sheath.

Caution: When the delivery sheath is removed, it must be done carefully by enlarging field of view for fluoroscopy. Operation without care such as quick removal without checking fluoroscopic image may cause the tip being captured by stent skeleton and result in deformation of stent skeleton and/or implanted stent graft migration, which may lead to serious adverse events. If delivery sheath is pulled back on the lesser curvature side of aortic arch, special attention is required.

- If the proximal end of the stent graft reaches zone 0, through and through guidewire should kept sagging inside of ascending aorta when delivery sheath is removed. If the through and through guidewire is tensioned, the stent graft may move to the distal side. When the through and through guidewire is removed, be careful not to tension it.
- When the proximal end of the stent graft reaches to Zone 1 or more proximal side, the pulses of both right and left carotid arteries shall be checked by palpation or other ways immediately after placement of the stent graft. When a pulse cannot be detected, the left common carotid artery or brachiocephalic artery can be covered for some reason. Appropriate treatment should be performed promptly.

- When multiple stent grafts are implanted, repeat the same procedure. When 2nd or later stent graft is inserted and removed, exercise care to prevent the delivery sheath from interfering with the implanted stent graft.

Caution: When going through previously implanted stent grafts which is placed at strongly tortuous vessel, especially careful operation is required, as the risk of interfering skeleton by delivery sheath is increased. [It may cause deformation of stent skeleton and/or implanted stent graft migration, which may lead to serious adverse events.]

- Insert an angiographic catheter from the sheath introducer at the secondary access site, perform angiography at required sites, and check to see that the stent graft is implanted to the planned position and is sufficiently expanded, and no endoleak is observed. Check to see that the blood flow in the main branch vessels that are not planned to be covered is adequate.
- If the blood flow in the main branch vessels that are not planned to be covered is inadequate, appropriate treatment should be performed promptly.
- If the expansion of the stent graft is inadequate, if endoleak of Type I or Type III is observed, or if necessary, appropriate treatment such as expansion using a balloon catheter, coil embolization, implantation of an additional stent graft, and more should be performed.
- When expansion using a balloon catheter is performed, exercise care to prevent the stent graft from moving from the planned position, which is caused by the movement of the balloon catheter due to blood flow. When the stent graft does not reach Zone 0, it is recommended to expand the balloon catheter with use of a through and through guidewire by adjusting tension appropriately.
- When the stent graft reaches Zone 0 and expansion by balloon catheter is required, because the through and through guidewire cannot be tensioned, it is recommended to insert the balloon catheter to the planned site using a stiff guide wire and surely holding the stiff guide wire, expand the balloon catheter.

(4) Implantation of stent graft having fenestration(s)

- The method of implanting a stent graft having fenestration(s) is basically the same. Confirm the position of the fenestration(s) of the stent graft preoperatively and carefully. During operation, confirm the position of the fenestration(s) from positions of radiopaque markers and exercise caution not to unexpectedly cover the arch branch vessels.
- When the proximal end of the stent graft reaches the arch branch vessels that are not planned to be covered, check the blood flow of the arch branch vessel through immediate check of carotid artery pulses by palpation, immediate angiography. If the blood flow cannot be detected, appropriate treatment should be performed promptly.

Caution: Occlusion of the arch branch vessel may cause the risk of causing a serious event such as death, cerebral infarction.

6.7. Closing access site

After completion of stent graft implantation, remove the guidewires and all the concomitant devices such as sheath introducers and other devices at each site under X-ray fuluoroscopy according to the standard procedure, and perform suture, hemostasis, and disinfection at the access sites in an appropriate way.

7. Cautions for proper use

7.1 Important basic cautions

- This device shall be used always under X-ray fluoroscopy by physicians who are skilled in stent grafting and percutaneous transluminal angioplasty. In the case with the possibility of an adverse event or a life-threatening complication, stentgrafting shall be performed in a hospital where surgical measures can be taken at once.
- To use the concomitant medications and medical devices safely, before usage, read instruction for use of these medications or devices carefully and confirm there is no abnormality in medications or devices.
- If a resistance is felt while a guidewire, an introducer sheath, or a delivery catheter is inserted, stop insertion and find the cause of the resistance. [Because vessels and the delivery catheter may be damaged]
- **The results of the clinical trial of the similar medical device show that-the incidence of cerebrovascular accidents (cerebral infarction and cerebral hemorrhage) becomes higher by using the fenestrated specifications. Physicians who use fenestrated type must understand they have higher risk of cerebrovascular accidents compared to non-fenestrated conventional ones and shall pay special attention to this point.** Consequently, when the fenestrated one is selected, application assessment shall be done carefully such as considering

the risk of cerebrovascular accidents (cerebral infarction and cerebral hemorrhage). [For further information, refer to capture 10 “The results of clinical trial”]

- Because it is observed that the risk of aneurysm diameter expansion becomes higher 1 year or later period after implantation according to the results of the clinical trial of the similar medical device for a thoracic aortic aneurysm when the length of the normal vessel between the bifurcation of the left common carotid artery and aortic aneurysm is 21 mm or less (the length of the normal vessel between the bifurcation of the left subclavian artery and aortic aneurysm is 21 mm or less when the left subclavian artery is not covered), this device shall be carefully adapted and the follow-up after implantation shall be observed with extra care, such as CT imaging with contrast dye or more often assessment. (When and how follow-up should be done based on a protocol of each hospital. In the clinical trial of the similar medicaldevice, the first follow up was performed at discharge and surveillance was repeated after 3 months, 6 months, 12months, then yearly.)
- For the case of expanding the aortic aneurysm follow-up should be performed in a facility with a medical specialist, who has experience in aortic aneurysm treatment. In addition, the aneurysm diameter shall be observed through imaging diagnosis on a regular basis.

(1) Cautions before use

- It shall be ensured that all the devices used in the treatment including this device operate properly before use. It shall be ensured that this device is suitable for its intended use and procedure.
- Ensure if guidewire goes through smoothly inside of delivery sheath, as some guidewires become tight in combination with delivery sheath when the sheath goes through tortuous vessels. As the sheath delivery of this device should be done by through and through technique in principle, the use of stainless steel spring guidewire is not recommended.
- In case that the package is damaged or contaminated or an abnormality such as damage to the device is found, do not use it.
- This device shall be used immediately after opening the package.
- It shall be ensured that the size of this device is suitable and this device is compatible with concomitant devices before use. [It shall be ensured that from the anatomical viewpoint a stentgraft with the appropriate specification is selected by the preoperative imaging diagnosis.]
- All the operations shall be performed under aseptic conditions.
- Flushing shall be sufficiently performed with use of heparinized saline to replace it with the air in the delivery sheath before use. [It is recommended that the amount of heparinized saline to be used for flushing is 100 ml or more.]
- This device shall be immersed in a tray in which heparinized saline is poured or be slightly wiped with a piece of gauze with heparinized saline soaked before use to enhance the lubricity by the hydrophilic coating of the outer sheath. [If a dry outer sheath is inserted into a body, lubricity does not function and a resistance at insertion becomes larger, which may lead to poor operability and damage to blood vessels.]
- When this device is wiped with a piece of gauze, handle it carefully. Do not use alcohol cotton to wipe the surface of this device. [Failure to observe this may peel the hydrophilic coating on the surface, which leads to lower insertion performance of the catheter or which may damage the catheter.]

(2) Caution during implant procedure

- An appropriate anticoagulant and a vasodilator shall be administered before insertion of this device, and an appropriate anticoagulant shall be administered and blood pressure control shall be performed during the procedure. A systemic anticoagulant shall be used on the basis of hospital regulations or physician's decision, and if heparin is contraindicate, another anticoagulant shall be selected.
- When this device is moved forward and backward along a guidewire, exercise caution to prevent the outer sheath from kinking and blood vessels from being damaged.
- It shall be monitored that there is no abnormality with this device and the patient. [If an abnormality is detected, an appropriate treatment such as removal of this device in the state that the patient is safe shall be performed.]
- The posterior expansion in the stentgraft using a balloon catheter shall be carefully performed. [Balloon can be pushed back by the blood flow on expansion, which may lead to the migration of the stent graft.]

7.2. Interaction

Magnetic resonance imaging (MRI)

The results of nonclinical study using the similar medical device under the prescribed conditions of using MRI equipment, Twin Speed 1.5T, manufactured by GE indicate that this stent graft is compatible with MR imaging. The conditions are described as follows:

Magnetic field intensity: 1.5 T (tesla)
Gradient field: 400 G (gauss)/cm
MR imaging for 15 minutes or shorter at specific absorption rate (SAR) of 3.77 W/kg

- No migration of the stent graft is confirmed as the result of MRI shooting for 15 minutes in the nonclinical study under the MRI shooting conditions described above. The safety of this device is not assessed for MRI shooting with the magnetic field intensity of more than 1.5 T or the gradient field of 400 G/cm or higher.
- As a result of the MRI shooting in the nonclinical study with 3 stent grafts overlapped done in the nonclinical study under the MRI shooting conditions described above, an temperature increase of the stent section 3.19 degrees or less is observed.
- An artifact of up to 16.5 cm is observed at the edge of the stent graft as a result of the assessment of image artifacts in the nonclinical study under the MRI shooting conditions described above.

Caution: The above mentioned nonclinical study have been conducted using the similar medical device “Najuta Thoracic Stent Graft System”. A combination with another device is not tested.

7.3. Failure and adverse events

Potential failures and adverse events through use of this device are shown below. When any of the following failures and adverse events is observed, an appropriate treatment shall be immediately performed.

(1) Failures

The following failures may occur through use of this device.

- Difficulty in catheter operation
- Difficulty in release and deployment of stent graft
- Implanting position failure
- Implantation failure
- Twist or kink of stent graft
- Rupture of graft material
- Damage or deformation to stent graft skeleton
- Migration of stent graft
- Deformation of or damage to delivery system
- Concomitant balloon rupture
- Stent graft thrombosis

(2) Adverse events

The following adverse events may be encountered through use of this device.

-Vascular complication

- Thrombosis
- Thromboembolism
- Occlusion (artery and vein)
- Vascular dissection or perforation
- Occlusion of collateral vessel
- Vascular ischemia
- Tissue necrosis
- Amputation

-Neurological complication

- Either of paraplegia or paraparesis, or spinal cord ischemia with multiple symptoms
- Cerebrovascular accident
- Transient ischemic attack (TIA)

- Neuropathy
- Blindness

-Other adverse events

- Death
- Conversion to surgical operation
- Rupture of vessel/aneurysm expansion
- Endoleak
- Renal failure
- Infection and fever
- Blood loss/hemorrhage
- Gastrointestinal complication (bowel disease such as paralytic ileus, temporary ischemia, infarction, necrosis included)
- Intestinal ischemia
- Pulmonary complication
- Wound healing complications
- Edema
- Heart failure/myocardial infarction
- Immedicable high blood pressure
- Wound dehiscence
- Aortic fistula
- Pain
- Complication from anesthesia
- Impotence
- Coagulation disorder
- Tissue trauma
- Hypotension
- Hematoma
- Claudication
- Lymphatic complication/sequela
- Altered mental status
- Arrhythmia requiring new medication or treatment
- Erosion with fistula or pseudoaneurysm
- Allergy to this device, contrast media, or concomitant medication
- Excessive or inappropriate radiation exposure

7.4. Risks and Benefits

The hazards associated can be categorized as device related failure (eg, breakage of stent, vessel damage due to broken stent), vascular complication (eg,thrombosis, thromboembolism), neurological complication (eg, paraplegia, paraparesis, cerebrovascular accident), other adverse events (eg, endoleak, allergy). These risks of endovascular repair must be weighed against the risks associated with the current alternative treatments of thoracic aortic dicease. Implantation of the Najuta CMD Thoracic Stent Graft System is likely a less invasive procedure than open surgical repair. Therefore, clinical benefits to patients treated with this device are may include shorter anesthesia times, shorter operation times, reduced procedural blood loss, the incision is small and less pain by open surgical repair.

7.5. Application to pregnant and nursing women, and paediatrics

(1) Application to pregnant and nursing women

Application to pregnant and nursing women shall be contraindicated (refer to the "Contraindication " section).

(2) Application to pediatric patients

The safety and effectiveness of this device for pediatric patients have not been evaluated.

7.6. Other cautions

- When this device is disposed after use, be careful not to contaminate the surrounding environment. This device

should be disposed properly as medical waste to prevent infection from blood.

- This device is a physician-oriented product and shall be used under the direction of a physician. This device shall not be used for other purposes.
- Check to be sure that this device is not damaged, joints are not loosened, blood does not leak, etc. while using it on a regular basis.
- Organic solvents such as alcohol, disinfectants, fat emulsions shall not adhere to this device. Failure to observe this may affect the resin materials of this device and accordingly cause damage this device. 1.2)
- If a breakage such as cracking is found on this device or there is missing components such as tip, it shall be immediately replaced with new product.
- Among the cases requiring that the left subclavian artery is covered in using this device, for a patient with a fear of diameter of lesion expansion due to blood pressure from the left subclavian artery into the lesion, coil embolization at the origin of the left subclavian artery should be considered as necessary.
- It should be noted that necessary lead time for the same specification as back up is 4 weeks. (In case another specification or measurement should be done again, longer lead time is required)

8. Information for patient counselling

Physicians and medical staff should consider the following points when counselling the patient about this device and its procedure. Necessary and appropriate information should be provided to the patient by physicians and medical staff.

- Difference between endovascular repair and open surgery, especially the risk of each treatment.
- Risk and benefit of open surgery and endovascular repair, and other possible treatment for vascular disease.
- It is possible that additional endovascular treatment or conversion to open surgery is required.
- The long-term effectiveness and safety of endovascular repair using stent graft has not been established.
- Patients must receive postoperative follow up, including imaging of the device, even when the patient does not have, such as the symptoms of pain, paralysis, hoarseness.
- The patient has to inform medical staffs that he or she has implanted stent when he or she receives MRI.

The details and more information are described in KAWASUMI patient information leaflet. It is recommended that physicians or medical staff use the leaflet to provide necessary information to patients.
Furthermore, additional or specific risks must be discussed depending on patient`s clinical condition, medical history.

9. Imaging diagnosis

9.1. General

- Pre-operative assessment should be done by using the most recent image taken within maximum 6 months prior to operation.
- The patients, whose aortic aneurysm is treated by this device, should receive follow-up assessment. Computed tomography (CT/CTA) should be done for all the patients at least once a year, even if clinical symptoms such as pain, numbness or hoarseness are not observed, to confirm the state of the implanted stent graft and to evaluate the size of aneurysm. Multiaxial diagnosis is recommended to assess the state of aneurysm expansion.
- For the patients with renal disorder or allergy to contrast dye, MRI (magnetic resonance imaging) or Chest X-ray （from three direction; frontal, left lateral, 45°left anterior oblique position(LAO)） maging diagnosis is recommended.
- For patients with specific clinical findings (such as endoleak, expansion of aneurysm), an extensive assessment is necessary. Accordingly, an additional endovascular treatment, or conversion to thoracotomy should be considered, or more frequent follow up is required.
- For assessment of endoleak, Multi phase CT angiography detecting in variable time is recommended. Angiography should be done not only in early phase but also in delay phase. The angiography in delay phase should be started roughly 60 sec after completion of early imaging.

9.2. Contrast enhanced CT image for pre-treatment

- To confirm morphological application of this device or to select appropriate specification, high-precision contrast enhanced CTA data is necessary
- Conditions are bellow

- Transected image CT slice thickness ：2mm or less
- Imaging phase：Early phase, Delay phase※

※Imaging in delay phase is necessary only for follow up. The angiography in delay phase should be started roughly 60 sec after completion of early imaging.

- Others should be set up following protocol of each facility.

10. The results of clinical trial

In order to evaluate the efficacy and safety of thoracic aortic aneurysm repair with use of the similar medical device, Najuta Thoracic Stent graft System, a prospective multicenter clinical trial (the total number of implanting cases: 117) was performed in Japan for patients with thoracic aortic aneurysm.
This clinical trial (test group) was unblind, and the efficacy and safety was verified with the historical control data (past surgery results collected in the Japanese Adult Cardiovascular Surgery Database) as a control group. The safety verification was performed to the group to whom matching was conducted using the propensity score regarding the adaptation of stent graft and surgical operation.

Analysis of efficacy
Primary endpoint: survival rate at 12 months after aneurysm-related treatment
The survival rate at 12 months after aneurysm-related treatment of the test group was 97.3%. The rate of the control group (open surgery results) was 96.2%, and the test group was proved to be noninferior, which was resulted from the verification with the threshold of 10%. According to the above, the principal purpose of the efficacy of this device has been verified.

Analysis of safety
Secondary endpoint: Major complication incidence
Major complication incidence in the test group to whom matching was conducted was 7.5%, and the ratio in the control group (surgery results) to whom matching was conducted was 20.8%. The 95% confidence interval for the difference was -26.3 to -0.3, and the test group was proved to be superior.
Second endpoint: survival rate at 12 months postoperative
The survival rate at 12 months postoperative in the test group to whom matching was conducted was 96.2%, and the rate in the control group (open surgery results) to whom matching was conducted was 90.4%. The 95% confidence interval for the difference was -3.7 to -15.3, and the test group was not proved to be superior but the survival rate at 12 months postoperative in the test group was higher.

Analysis of utility
Operation time, ICU stay, start time of ingestion and hospitalization were compared between the test and control group to whom matching was conducted. As a result, the test group was superiorly ($P<0.01$ or $P=0.02$) shorter in Operation time, ICU stay and hospitalization. According to the above, the utility of the endovascular repair using this device was suggested to be superior to surgery.

Caution: The above mentioned clinical-trial have been conducted using the similar medical device “Najuta Thoracic Stent Graft System”.

Table 1. Major complication incidence of the similar medical device, Najuta Thoracic Sten

		Within 30 days after surgery			30 days to 12 months after surgery		
		Total	With fenestration(s)	Without fenestration(s)	Total	With fenestration	Without fenestration
All deaths		0.9% (1/117)	1.3% (1/79)	0.0% (0/38)	4.3% (5/117)	5.1% (4/79)	2.6% (1/38)
Aneurysm-related mortality		0.9% (1/117)	1.3% (1/79)	0.0% (0/38)	1.7% (2/117)	1.3% (1/79)	2.6% (1/38)
Cardiac disease requiring surgical treatment		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	0.0% (0/117)	0.0% (0/79)	0.0% (0/38)
Long-term artificial respiration requiring tracheotomy		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	1.7% (2/117)	1.3% (1/79)	2.6% (1/38)
New renal disease		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	1.7% (2/117)	2.5% (2/79)	0.0% (0/38)
Aortic fistula		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	0.0% (0/117)	0.0% (0/79)	0.0% (0/38)
Pressure on adjacent organs		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	0.0% (0/117)	0.0% (0/79)	0.0% (0/38)
Mesenteric ischemia		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	0.0% (0/117)	0.0% (0/79)	0.0% (0/38)
Paraplegia or paraparesis		1.7% (2/117)	1.3% (1/79)	2.6% (1/38)	0.9% (1/117)	1.3% (1/79)	0.0% (0/38)
Pulmonary embolism		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	0.9% (1/117)	1.3% (1/79)	0.0% (0/38)
Cerebrovascular disease	Cerebral infarction	6.0% (7/117)	7.6% (6/79)	2.6% (1/38)	0.0% (0/117)	0.0% (0/79)	0.0% (0/38)
	Cerebral hemorrhage	0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	3.4% (4/117)	5.1% (4/79)	0.0% (0/38)
Multiple organ failure		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	0.0% (0/117)	0.0% (0/79)	0.0% (0/38)
Ischemia of lower limb		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	0.0% (0/117)	0.0% (0/79)	0.0% (0/38)
Aneurysm rupture		0.0% (0/117)	0.0% (0/79)	0.0% (0/38)	0.0% (0/117)	0.0% (0/79)	0.0% (0/38)
Vascular injury (vascular injury, aortic dissection)		5.1% (6/117)	2.5% (2/79)	10.5% (4/38)	0.9% (1/117)	1.3% (1/79)	0.0% (0/38)

11. Stock and storage method, validity period

(1) Stock and storage method

This device shall be stored away from direct sunlight, UV rays, high temperature, and high humidity with careful attention to water leakage.

(2) Valid period and expiration date

Refer to the expiration date described on the box. [By self-certification (our data)]

12. Product Information

- 1 set/box
- Ethylene oxide sterilization
- Made in Japan

13. Manufacturer and EU representative information

SB-KAWASUMI LABORATORIES, INC.
3-25-4 Tonomachi, Kawasaki-ku, Kawasaki-shi, Kanagawa 210-8602, Japan
TEL: +81-44-589-8070

EC REP Medical Technology Promedt Consulting GmbH Altenhofstrasse 80, 66386 St. Ingbert, Germany

The description of symbols.

	Manufacturer		Consult instruction for use
EC REP	Authorized representative in the European Comminity		Non-pyrogenic
	Date of manufacture		Do not resterilize
	Use-by date		Do not use if package is damaged
LOT	Batch code		Fragile, handle with care
REF	Catalogue number		Keep away from sunlight
STERILE EO	Sterilized using ethylene oxide		Keep dry
	Do not re-use		Right side up
	Handle with care		Do not use blades to open
QTY	Quantity		Temperature limit
	Caution	SBS	Double sterile barrier system
MR	MR Conditional		

14. Material

The following materials and substances are used for implanted devices.

No.	Component	Material	Specification	Blood contact
(1)	Stent skeleton	Stainless steel	A)	◎
(2)	Fixing Ring	Stainless steel (SUS316L)	B)	◎
(3)	Radiopaque maker			
(4)	Graft	Polytetrafluoroethylene,	C)	◎
(5)	Suture	PolyVinylidene DiFluoride	-	◎

A) Stent graft (Stent skeleton)

Material	Stainless steel
Standards of medical materials (JIS, ISO and ASTM)	ISO 5832-1: Implants for surgery -Metallic materials -Part 1: Wrought stainless steel

B) Stent graft (Fixing Ring, Radiopaque maker)

Material	Stainless steel (SUS316L)
Public standards of other	JIS G 4305 Cold-rolled stainless steel plate, sheet and strip

C) Stent graft (Graft)

Material	Polytetrafluoroethylene
CAS No., USAN name, CSCL notification No.	CAS No. 9002-84-0

15. Notice to the user and/or patient

If the user and / or patient is aware of an incident that has occurred in relation to the device, it should report to the manufacturer and the competent authority of the Member State in which the user and / or patient was established.